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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/486,904	03/03/2000	JOHN R. SNYDER	3220-66107	9526

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EXAMINER

HELMER, GEORGIA L

ART UNIT	PAPER NUMBER
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1638

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DATE MAILED: 09/23/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Applicati n No.

09/486,904

Applicant(s)

SNYDER ET AL.

Examiner

Georgia L. Helmer

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on 19 June 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 9 and 20-25 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 9 and 20-25 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

Status of the Claims

1. The Office acknowledges receipt of Applicants Response; dated 19 June 2003, paper number 20.
2. Applicant has cancelled claims 1-8, 15-19 and amended claims 9, 20, 21, and 23-24. Claim 25 has been added. Claims 9 and 20-25 are pending and are examined in this Office Action.
3. This action is made FINAL necessitated by Applicant's amendment.
4. All rejections not addressed below have been withdrawn.
5. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Information Disclosure Statement

6. It is noted that Applicant has included reference articles with this Response. However, a proper submission of references must comply with 37 CFR 1.97 and include a filled-out PTO 1449 for consideration by the Office. Applicant must supply the appropriate 1449 in response to this action, or the response will be considered nonresponsive.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 9 and 20-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 9 ,

- In claim 9 , line 5, “gene” is unclear because a “gene” implies a DNA sequence that exists in nature and includes coding and noncoding regions, as well as all regulatory sequences associated with expression. This rejection remains for reasons of record. Applicant can obviate this rejection by replacing “of a structural gene coding for” with “encoding a compound...”.
- Also in claim 9, line 7, “structural gene” needs to be replaced with “coding sequence” for the same reason.
- In claim 9, line 16, “economical quantities” remains unclear for reasons of record.

Applicant traverses, stating primarily (response, p. 5) that the term “economical quantities” refers to a compound that is produced in sufficient quantities that the value of the extracted compound exceeds the costs associated with standard production and extraction methods. Applicant’s traversal has been considered and is unpersuasive, because no standard is given for “sufficient quantities”, or “the costs associated with standard production and extraction methods”. Since it is not known what “standard production costs” are, one cannot assess what quantity would be economical.

Claim Rejections - 35 USC § 112-1 Enablement

9. Claims 9 and 20-25 remain rejected under 35 U.S.C. 112, first paragraph. To the extent that this is a new rejection, it is necessitated by Applicant's amendment. The specification, while being enabling for a method of producing a compound that is not detrimental to the plant, is not enabling for a compound detrimental to the plant, The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicant claims any compound produced by a structural gene, where the compound is detrimental to the plant, expressing this compound, and extracting this compound in economic quantities.

Applicant teaches a glucuronidase and a bar resistance gene and expressing these genes, which are benign to the plant, a transformed plants. Applicant teaches extracting the glucuronidase for analysis of expression levels.

The state of the art is that one skilled in the art can readily make DNA constructs containing a structural gene encoding a compound, transform these into plants and express them with a reasonable expectation of success. However, expressing structural genes encoding a compound detrimental to the plant, such as barnase, is more unpredictable. Barnase is compound detrimental to the plant and expression is lethal to cells and tissues in which it occurs. Therefore expression of the gene encoding

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this detriment compound must be regulated in order to avoid killing all cells expressing it. (see Gutterson, US 6,392,119, column 14, lines 40-55). Recombinase mediated excision of appropriately flanked DNA sequences is variable and yields chimeric phenotypes having both recombined and unrecombined DNA (Gidoni, D. et al, Supplement to Plant Molecular Biology Reporter 18:2, S 03-40; ISPMB abstracts, June 18-24, 2000)(U). Recent studies (Gidoni, D et al (2001) Euphytica 121: 145-156. see pages 146 and 152) of embryonal recombination and germline inheritance of recombined tobacco loci show variable recombination efficiencies. Vergunst (Nucleotide. Acids. Research, 1998, vol 26, pages 2729-2734, see all of page 2733) shows unpredictability using the recombinase system as evidenced by instability of recombinants and phenotypic "escapes". The claimed methods require use of site-specific recombination systems to delete appropriately flanked DNA sequences.

Applicant traverses, stating primarily that recent work has demonstrated that site specific recombinases can be nearly 100% efficient. Applicant cites Xuo et. al. (2001) Nature biotechnology 19 : 157-161, as teaching that all 19 of the Arabidopsis thaliana lines created using a Cre/lox mediated excision system underwent excision. Applicant's traversal has been considered and is unpersuasive. For a post-filing date reference to be used as evidence of enablement as of the filing date, the reference must contain exactly the same method as the instant case. Zuo teaches (p. 157) the use of Cre/lox system in Arabidopsis thaliana plants transformed by Agrobacterium mediated T-DNA stable transformation. The cre recombinase is under the control a an estradiol-receptor

based transactivator. This is a chemically inducible system for expression of cre. Cre activity catalyses recombinase to excise the blocking sequence contained between two lox sites to place the glo-9 promoter operationally in front of the gfp coding sequence, to produce gfp expression. The instant case teaches intracellular use of PEG-mediated transformation of corn or rice protoplasts with plasmids containing either Ubi-FLP (constitutive promoter) or Heat-Shock-FLP (Inducible promoter) to express FLP recombinase, and second plasmid containing a ubiquitin promoter operably linked to two FRT sites flanking a coding sequence and followed by a β -glucuronidase coding sequence. FLP catalysis at the FRT sites causes excision of β -galactosidase and places the Ubi promoter operably linked to the β -glucuronidase coding sequence to allow expression of β -glucuronidase. Zuo is different in many ways from the instant case, and does not provide post filing date evidence of the enablement of the instant case.

Applicant traverses, stating primarily that recent work has demonstrated that site specific recombinases can be nearly 100% efficient. Applicant cites Luo et. al. (2000) The Plant Journal 23(3): 423-430, as showing similar success (to Zuo) with FLP/FRT. Applicant's traversal has been considered and is unpersuasive. For a post-filing date reference to be used as evidence of enablement as of the filing date, the reference must contain exactly the same method as the instant case. Luo teaches Agrobacterium mediated T-DNA transformation of Arabidopsis thaliana plants with a coding sequence controlled by the 35SCaMV promoter and the omega translational enhance. Production of FLP catalyzes excision of FRT-flanked bcp1 antisense

sequence. The presence of the *bcp1* antisense causes male sterility; removal of *bcl1* restores fertility to the plant.

The instant case teaches intracellular use of PEG-mediated transformation of corn or rice protoplasts with plasmids containing either Ubi-FLP (constitutive promoter) or Heat-Shock-FLP (Inducible promoter) to express FLP recombinase, and second plasmid containing a ubiquitin promoter operably linked to two FRT sites flanking a coding sequence and followed by a β -glucuronidase coding sequence. FLP catalysis at the FRT sites causes excision of β -galactosidase and places the Ubi promoter operably linked to the β -glucuronidase coding sequence to allow expression of β -glucuronidase. Luo is different in many ways from the instant case, and does not provide post filing date evidence of the enablement of the instant case.

Therefore, without further guidance, it is unpredictable that one skilled in the art would be able to express in a plant a structural gene encoding a compound detrimental to the plant, as Applicant has provided no guidance on how to predictably eliminate inoperable embodiments from a virtually ad infinitum of possibilities other than by random trial and error, which is excessive experimentation and an undue burden.

Applicant claims extracting a compound detrimental to the plant, and "in economic quantities". Since "in economic quantities" is undefined, it is impossible to determine what this term means, and claims to economic quantities are considered nonenabled.

In view of the breadth of the claims (any plant, any compound detrimental to the plant, any extraction, and extraction in economic quantities), the lack of guidance in the specification, the lack of working examples, undue trial and error experimentations would be required to enable the invention as commensurate in scope with the claims.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

11. Claims 9 and 20 – 25 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Kilby, NJ et al; (1995) Plant Journal 8: 637-652 (AR), in view of Odell et al (AA) and Kilby, NJ et al (1993) Trends in Genetics, 9: 413-421, for reasons of record. To the extent that this a new rejection, it is necessitated by Applicant 's amendment.

Applicant's previously amended claim 9 recites "expressing the compound detrimental to the plants and extracting the compound in economical quantities".

Applicant traverses, stating primarily (response, p. 6) that the term "economical quantities" refers to a compound that is produced in sufficient quantities that the value of the extracted compound exceed the costs associated with standard production and extraction methods.

Applicant's traversal has been considered and is unpersuasive because although Applicant has amended the claims to recite "extracting the compound in economical quantities", which Applicant says refers to a compound that is produced in sufficient quantities that the value of the extracted compound exceed the costs associated with standard production and extraction methods. Even though Applicant has given this "definition", this does not teach what "standard production costs are". And because no standard production costs are given, one cannot assess what quantities would be economical.

Remarks

11. No claim is allowed.
12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

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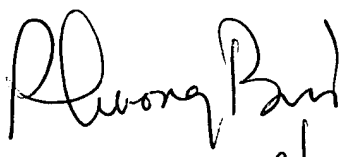
extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Georgia L. Helmer whose telephone number is 703-308-7023. The examiner can normally be reached on 8:30 - 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on 703-306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Georgia Helmer PhD
Patent Examiner
Art Unit 1638
September 22, 2003


PHUONG T. BUI
PRIMARY EXAMINER
9/22/03